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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,911	10/21/2005	Kurt Eyer	LP-2009	1089

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EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,911	EYER ET AL.	
	Examiner	Art Unit	
	SUSAN HANLEY	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

Applicant's election of species B in the reply filed on 2/5/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's response is entirely directed to paraphrasing the restriction requirement. Applicant has not directed any argument against the content of the restriction itself.

However, upon further consideration, the species election is withdrawn and all of the claims will be examined.

Claims 1-18 are presented for examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in

order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omura et al. (US 4,107,297; cited in the IDS filed 1/4/08) in view of Hershberger et al. (US 4,637,981), Borghi et al. (US 5,135,857) and Nabais (1995).

Omura discloses the recovery of Staurosporine (AM-2282) from a fermentation broth. For example, a fermentation broth containing staurosporine can be separated into microbial bodies and filtrate by filtration or without separating the broth into solids and liquid. The latter method is based on the physical and chemical characteristics of staurosporine which is fat-soluble. Omura provides an example wherein a culture broth is adjusted to pH 10 and extracted with butyl acetate. The extract is concentrated *in vacuo* to a small volume and transferred into water at pH 10. The aqueous mixture is extracted with ethyl acetate. The organic layer is evaporated to obtain the product and then chromatographed in silica gel (col. 6, lines 40-60). The crude product is recrystallized to provide pale yellow needles (col. 7, lines 1-4; as in claim 17). Omura states that staurosporine recovery can be achieved by "known methods for separating antibiotics" (col. 6, lines 41-42). Claims 2-11, 13, 14 and 18 are rejected because they limit steps that are indicated as optional in claim 1. For the purposes of this rejection, the claims are interpreted that the optional steps are not performed.

Omura does not disclose that staurosporine is recovered from a fermentation broth by diluting the broth with a water-miscible organic solvent, ultrafiltration of the diluted broth, concentration and adjustment of the pH to at least 8.5 to precipitate the product which is collected by centrifugation.

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Hershberger discloses that a broth containing a glycopeptide antibiotic, factor G, is diluted with a water miscible organic solvent such as acetone, acidified and filtered to separate the mycelium and other insolubles. The filtration can be accomplished with dichotomous earth or other commercially available filter aids. Separation can also be accomplished by centrifugation. After separation, the liquid portion is evaporated to remove the solvent. Hershberger reports that the disclosed antibiotic, factor G, was separated on a resin and the eluate was precipitated as the free base at pH 6.5 to 7.5. Hershberger teaches that, alternatively, factor G can be recovered from the fermentation medium by conventional isolation procedures such as absorption on a suitable ion exchange resin followed by chromatographic separation (col. 9, lines 31-65).

Nabais discloses that ultrafiltration is an effective method to separate the solids from a broth to effect the recovery of clavulanic acid (abstract).

Borghi discloses that the antibiotic, teicoplanin, can be isolated from the extract of a mycelium by techniques known in the art including extraction with solvents, precipitation with non-solvents or by changing the pH of the solution, partition chromatography, reverse phase chromatography, affinity chromatography and the like (col. 6, lines 50-57). Thus, Borghi establishes that methods for the recovery of antibiotics from biological sources are well established in the art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recover staurosporine from a fermentation broth by diluting the broth with a water-miscible organic solvent, ultrafilteirng and concentrating the diluted broth, and then adjusting the pH of the concentrate to at least 8.5 to precipitate and collect the product by centrifugation. The ordinary artisan would have been motivated to do so because in Ex parte Kubin, 83 USPQ2d 1410 (Bd. Pat. App. & Int. 2007), the Board found that "when there are a finite number of identified,

predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense."

The case was directed to an isolated nucleic acid molecule. The claim stated that the nucleic acid encoded a particular polypeptide. The encoded polypeptide was identified in the claim by its partially specified sequence, and by its ability to bind to a specified protein. A prior art patent to Valiante taught the polypeptide encoded by the claimed nucleic acid, but did not disclose either the sequence of the polypeptide, or the claimed isolated nucleic acid molecule. However, Valiante did disclose that by employing conventional methods such as those disclosed by a prior art laboratory manual by Sambrook, the sequence of the polypeptide could be determined, and the nucleic acid molecule could be isolated. In view of Valiante's disclosure of the polypeptide, and of routine prior art methods for sequencing the polypeptide and isolating the nucleic acid molecule, the

Board found that a person of ordinary skill in the art would have had a reasonable expectation that a nucleic acid molecule within the claimed scope could have been successfully obtained.

Relying on In re Deuel, 51 F.3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995), appellant argued that it was improper for the Office to use the polypeptide of the Valiante patent together with the methods described in Sambrook to reject a claim drawn to a specific nucleic acid molecule without providing a reference showing or suggesting a structurally similar nucleic acid molecule. Citing KSR, the Board stated that "when there is motivation to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the

product not of innovation but of ordinary skill and common sense." The Board noted that the problem facing those in the art was to isolate a specific nucleic acid, and there were a limited number of methods available to do so. The Board concluded that the skilled artisan would have had reason to try these methods with the reasonable expectation that at least

one would be successful. Thus, isolating the specific nucleic acid molecule claimed was "the product not of innovation but of ordinary skill and common sense."

In the instant case, the ordinary artisan would have recognized that there are a finite number of art-recognized solutions for the isolation of an antibiotic from a fermentation broth. Hershberger discloses alternative methods for the initial treatment of the broth. The dilution, filtration concentration steps taught by Hershberger are conventional in the art and the ordinary artisan would have had a reasonable expectation that said would be at least comparable to the initial broth extraction steps employed by Omura. Likewise, the ordinary artisan would have been motivated to substitute a method of changing the pH of the concentrate to precipitate staurosporine for the extraction/chromatography steps taught by Omura because Borghi established that said methods were well-known, finite, alternatives in the art of antibiotic isolation. The ordinary artisan would have been motivated to employ a pH of least 8 or 10 (claim 15) to precipitate staurosporine because staurosporine, like the glycopeptide taught by Borghi, would exist as a free amine at a basic pH and precipitate from the solution.

The ordinary artisan would have been motivated to employ ultrafiltration for the filtering step taught by Hershberger because it is a commercially available filter aid that is conventional in the art for searing the insoluble material from a broth for the recovery of an antibiotic. The ordinary artisan would have had a reasonable expectation that he or she could successfully employ an ultrafiltration method to separate insolubles from a broth containing staurosporine becasue fermentation broths contain essentially the same components (e.g., proteins, microorganisms, small molecules, etc.).

Therefore, the isolation of staurosporine from a fermentation broth is obvious because the field of antibiotic isolation from a broth is well developed and there are a finite number of identified, predictable solutions that a person of ordinary skill would have good reason to pursue. The substitution of the known options to effect antibiotic purification are within the technical grasp of the ordinary artisan. Hence, the claimed method is not of one of innovation but of ordinary skill and common sense.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/
Primary Examiner, Art Unit 1651

/Susan Hanley/
Examiner, Art Unit 1651